Health Technology Briefing
May 2025

Baxdrostat for treating uncontrolled hypertension including resistant hypertension

Company/Developer	AstraZeneca UK Limited

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 37919	NICE ID: Not available	UKPS ID: 673377

Licensing and Market Availability Plans

Currently in phase III clinical trials

Summary

Baxdrostat is in clinical development for the treatment of uncontrolled hypertension including resistant hypertension (high blood pressure). The cause of high blood pressure is not always clear, however, it can be due to lifestyle factors such as having a poor diet, being overweight, smoking and eating too much salt. Sometimes it can be caused by medications or other issues such as vascular disease, kidney disease or sleep apnoea. Resistant hypertension is defined as blood pressure that remains high even after using three or more different types of medication. It does not always have symptoms and when they do occur, they include headaches, shortness of breath and chest pain. Uncontrolled or resistant hypertension substantially increases the risk of a heart attack, stroke and kidney failure.

Baxdrostat works by inhibiting an enzyme called aldosterone synthase. Aldosterone is a hormone that plays a crucial role in regulating blood pressure by controlling the balance of salt and water in the body. By blocking the production of aldosterone, baxdrostat aims to lower blood pressure in patients who have not responded well to other treatments. Since resistant hypertension is unresponsive to current medications, new treatments are required. Baxdrostat is taken once a day orally. If licenced, baxdrostat would offer a new treatment option for people with uncontrolled hypertension including resistant hypertension.

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.

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Proposed Indication

Adults for the treatment of uncontrolled hypertension including resistant hypertension.[1]

Technology

Description

Baxdrostat (CIN-107) is a highly selective, oral small molecule aldosterone synthase inhibitor, the enzyme responsible for the synthesis of aldosterone in the adrenal glands.[2] Aldosterone plays a vital role in the regulation of sodium transport and sodium-potassium linked transport across all epithelial structures. Inhibition of synthesis of aldosterone leads to a reduction in the reabsorption of sodium and secretion of potassium, and this in turn leads to a decrease in chronic blood volume ultimately resulting in decreased blood pressure values.[3] Substantial evidence indicates that aldosterone excess is very common in patients with resistant hypertension.[4] Baxdrostat reduces plasma aldosterone levels in a dose-dependent manner while having no significant effect on cortisol levels, demonstrating high selectivity for aldosterone synthase inhibition over that of 11β-hydroxylase, the enzyme that synthesizes cortisol.[2]

Baxdrostat is in clinical development for adults with uncontrolled hypertension including resistant hypertension who are taking 2 or more hypertensives. In the phase III clinical trials (NCT06034743, NCT06168409, NCT06344104) baxdrostat 1mg or 2mg is given orally once a day for 12 weeks.[1,5,6]

Key Innovation

The development of ASIs has shown promise in treating resistant hypertension by decreasing aldosterone production. Previous ASIs faced limitations, such as reduced efficacy, unfavourable side effects and inhibited cortisol synthase. Baxdrostat, exhibits greater selectivity for aldosterone synthase compared to existing ASIs.[7] Baxdrostat was observed to significantly lower aldosterone levels without affecting cortisol levels, across a wide range of doses.[8,9]

If licenced, baxdrostat would offer an additional treatment for patients with uncontrolled hypertension including resistant hypertension who are already taking 2 or more hypertensives.

Regulatory & Development Status

Baxdrostat does not currently have marketing authorisation in the EU/UK for any indication.

Baxdrostat as a monotherapy in a phase II trial for primary aldosteronism.[10]

Baxdrostat in combination with dapagliflozin is also in phase III/II trials for:[10]

- Prevention of heart failure
- Chronic kidney disease with hypertension

Patient Group

Disease Area and Clinical Need

Resistant hypertension is defined as blood pressure that remains above the therapeutic goal of 140/90 mmHg despite concurrent use of at least three antihypertensive agents of different classes, including a diuretic, with all agents administered at maximum or maximally tolerated doses.[11] High blood pressure is

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very common, especially in older adults, and there are usually no symptoms. Rarely, high blood pressure can cause symptoms such as headaches, blurred vision and chest pain. Primary hypertension does not have a clear cause.[12] Things that can increase the chance of having high blood pressure are older age, unhealthy diet, being overweight, smoking and eating too much salt.[13] Secondary hypertension has at least one cause that healthcare providers can identify. Common causes of secondary hypertension include certain medications such as immunosuppressants and oral contraceptives, kidney disease, sleep apnoea, drug use and vascular disease.[12] Over time, uncontrolled hypertension damages the arteries, contributing to their stiffening. When the arteries become narrower and less flexible, the heart must work harder to move blood through the body. Resistant hypertension substantially increases the risk of heart attack, stroke and kidney failure.[14]

A report by the department of health & social scare (2023/24) shows 9,350,858 of the population in England have hypertension.[15,16] In England (2023-2024), there were 53,707 finished consultant episodes (FCEs) for essential (primary) hypertension (ICD-10 code I10.X), leading to 44,598 admissions, 3,618 day cases and 44, 272 FCE bed days.[17]

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) state if hypertension is not controlled in adults taking the optimal tolerated doses of an angiotensin-converting enzyme inhibitor or an angiotensin receptor blocker plus a calcium-channel blocker and a thiazide-like diuretic they should be regarded as having resistant hypertension. For people with confirmed resistant hypertension, NICE currently recommends adding a fourth antihypertensive drug as step 4 treatment, further diuretic therapy with low-dose spironolactone for adults who have a blood potassium level of 4.5 mmol/l or less or alpha-blockers or beta-blockers for adults who have a blood potassium level of more than 4.5 mmol/l.[18]

Clinical Trial Information

Trial	**BaxHTN; NCT06034743;** A randomised, double-blind, placebo-controlled, parallel group study to assess the efficacy and safety of baxdrostat in participants with uncontrolled hypertension on two or more medications including participants with resistant hypertension **Phase III -** active, not recruiting **Location(s) -** 14 EU countries, UK, USA, Canada and other countries **Primary completion date -** June 2025
Trial Design	Randomised, parallel assignment, quadruple blind, placebo-controlled
Population	N=796 (actual); adults with mean sitting systolic blood pressure (SBP) on automated office blood pressure measurement (OBMP) ≥ 140 mmHg at screening and be taking at least 2 antihypertensive medications at maximum tolerated dose; aged 18 and over.
Intervention(s)	• Baxdrostat 2mg oral, once daily (QD) • Baxdrostat 1mg oral QD
Comparator(s)	Matched placebo
Outcome(s)	Primary outcome: • Change from baseline in seated SBP for 2 mg baxdrostat

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	• Change from baseline in seated SBP for 1 mg baxdrostat See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-
Trial	**Bax24:** NCT06168409; A randomised, double-blind, placebo-controlled, parallel group study to assess the effect of baxdrostat on ambulatory blood pressure in participants with resistant hypertension **Phase III** - active, recruiting **Location(s)** - 9 EU countries, UK, USA, Canada and other countries **Primary completion date** - September 2025
Trial Design	Randomised, parallel assignment, quadruple blind, placebo controlled
Population	N=212 (estimated) adults with mean seated SBP on automated OBPM of ≥ 140 mmHg and < 170 mmHg at screening and taking at least 3 antihypertensives at a maximum tolerated dose; aged 18 and over
Intervention(s)	Baxdrostat 2mg oral QD
Comparator(s)	Matched placebo
Outcome(s)	Primary outcome: Change from baseline in ambulatory 24-hour average SBP See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-
Trial	**BaxAsia**; NCT06344104**;** A double-blind, randomised, placebo-controlled, multicentre study evaluating the efficacy and safety of baxdrostat in participants with uncontrolled hypertension on two or more medications including participants with resistant hypertension **Phase III** - recruiting **Location(s)** - Australia, China, and other countries **Primary completion date** - May 2026
Trial Design	Randomised, parallel assignment, quadruple blind, placebo-controlled
Population	N=300 (estimated); adults with SBP ≥ 140 mmHg on OBPM at screening and taking at least 2 antihypertensives at maximum tolerated dose; aged 18 and over.
Intervention(s)	• Baxdrostat 2mg oral QD • Baxdrostat 1mg oral QD
Comparator(s)	• Matched placebo
Outcome(s)	Primary outcome: Change from baseline in seated SBP at week 12

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	• See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of baxdrostat is not yet known.

Relevant Guidance

NICE Guidance

- NICE clinical guideline. Hypertension in adults: diagnosis and management (NG136). August 2019, last updated November 2023.
- NICE quality standard. Hypertension in adults (QS28). March 2013, last updated: September 2015
- NICE interventional procedures guideline. Alcohol-mediated perivascular renal sympathetic denervation for resistant hypertension (IPG801). March 2025.
- NICE interventional procedures guideline. Percutaneous transluminal renal sympathetic denervation for resistant hypertension (IPG754). March 2023.
- NICE interventional procedures guideline. Implanting a baroreceptor stimulation device for resistant hypertension (IPG533). October 2015.

NHS England (Policy/Commissioning) Guidance

No relevant guidance identified

Other Guidance

- The Task Force for the management of elevated blood pressure and hypertension of the European Society of Cardiology (ESC) Endorsed by the European Society of Endocrinology (ESE) and the European Stroke Organisation (ESO). ESC Guidelines for the management of elevated blood pressure and hypertension. 2024.[19]
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